

What is claimed is:

1. A vector comprising a coding sequence and a magnum-specific promoter in operational and positional relationship to express said coding sequence in tubular gland cells of the avian oviduct.
2. The vector of claim 1, wherein said magnum-specific promoter is a segment of the *ovalbumin* promoter region, wherein said segment is sufficient for effecting expression of the coding sequence in the tubular gland cells of an avian oviduct.
3. The vector of claim 2, wherein the segment of the *ovalbumin* promoter region comprises a segment of the 5'-flanking region of the *ovalbumin* gene which is from about 0.88 kb to about 1.4 kb in length and includes both the steroid-dependent regulatory element and the negative regulatory element.
4. The vector of claim 1, wherein the vector is retroviral and wherein said coding sequence and said magnum-specific promoter are both positioned between the 5' and 3' LTRs of the retroviral vector.
5. The vector of claim 4, wherein the retroviral vector is derived from the avian leukosis virus.
6. The vector of claim 1, further comprising a second coding sequence and an internal ribosome entry site element, wherein said internal ribosome entry site element is positioned between the first and second coding sequences.

7. The vector of claim 6, wherein the protein encoded by the second coding sequence is capable of providing post-translational modification of the protein encoded by the first coding sequence.

5 8. The vector of claim 1, further comprising a signal peptide coding sequence which is operably linked to said coding sequence, so that upon translation in a cell, the signal peptide will direct secretion of the protein expressed by the vector.

9. The vector of claim 1, further comprising a marker gene, wherein said marker gene  
10 is operably linked to a constitutive promoter selected from the group consisting of the *Xenopus laevis ef-1 $\alpha$*  promoter, the *HSV tk* promoter, the CMV promoter, and the  $\beta$ -*actin* promoter.

10. A targeting vector for insertion of a promoter-less minigene into a target gene in an  
15 avian, comprising  
a coding sequence;  
at least one marker gene, wherein said marker gene is operably linked to a  
constitutive promoter and can be used for identifying cells which have integrated the  
targeting vector; and  
20 targeting nucleic acid sequences which correspond to sequences flanking the point  
of insertion in the target gene, wherein said targeting nucleic acid sequences direct  
insertion of the targeting vector into the target gene.

11. The targeting vector of claim 10, wherein said target gene is an endogenous gene  
25 that is expressed in the avian oviduct.

12. The targeting vector of claim 11, wherein the target gene is selected from the  
group consisting of *ovalbumin*, *lysozyme*, *conalbumin*, *ovomucoid*, and *ovomucin*.

13. The targeting vector of claim 10, wherein the point of insertion is in the 5' untranslated region of the target gene.

5 14. The targeting vector of claim 10, wherein the point of insertion is in the 3' untranslated region of the target gene and wherein the targeting vector further comprises an internal ribosome entry site element positioned directly upstream of said coding sequence.

10 15. The targeting vector of claim 10, further comprising a signal peptide coding sequence which is operably linked to the first coding sequence, so that upon translation in a cell, the signal peptide will direct secretion of the protein expressed by the first coding sequence.

15 16. The targeting vector of claim 10, further comprising a second coding sequence and an internal ribosome entry site element, wherein said internal ribosome entry site element is positioned between the first and second coding sequence.

20 17. The targeting vector of claim 16 wherein the protein encoded by the second coding sequence is capable of providing post-translational modification of the protein encoded by the first coding sequence.

25 18. A vector for insertion of a promoter-less minigene into a target gene, comprising the targeting vector of claim 10, wherein said targeting vector further comprises a second marker gene which is operably linked to a second constitutive promoter, said second marker gene being positioned outside said targeting nucleic acid sequences so that, upon insertion of the promoter-less minigene into the target gene, the second marker gene will not be inserted.

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19. A transgenic bird having a transgene in the genetic material of its germ-line tissue, wherein the transgene comprises an exogenous gene and a promoter, in operational and positional relationship to express said exogenous gene, and said exogenous gene is expressed in the tubular gland cells of the avian oviduct of the transgenic bird.

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20. The transgenic bird of claim 19, wherein the promoter is a magnum-specific promoter.

10 21. The transgenic bird of claim 19, wherein the transgenic bird is selected from the group consisting of chickens and turkeys.

15 22. A transgenic bird having a transgene in the genetic material of its germ-line tissue, wherein the transgene comprises an exogenous gene which is positioned in either the 5' untranslated region or the 3' untranslated region of an endogenous gene so that the regulatory sequences of the endogenous gene direct expression of the exogenous gene.

20 23. The transgenic bird of claim 22, wherein said endogenous gene is selected from the group consisting of *ovalbumin*, *lysozyme*, *conalbumin*, *ovomucoid*, and *ovomucin*.

24. The transgenic bird of claim 22, wherein the transgenic bird is selected from the group consisting of chickens and turkeys.

25 25. An <sup>unreferred</sup> egg of an avian species containing protein exogenous to the avian species.

26. A method for the stable introduction of an exogenous coding sequence into the genome of a bird, comprising:

*HL  
B3 a*

introducing the vector of claim 1 into avian embryonic blastodermal cells, wherein the vector is randomly inserted into the avian genome.

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27. A method for producing an exogenous protein in an avian oviduct, comprising: providing a vector that comprises a coding sequence and a promoter operably linked to said coding sequence, wherein said promoter can effect expression of the coding sequence in the tubular gland cells of an avian oviduct; creating transgenic cells by introducing said vector into avian embryonic blastodermal cells, wherein the vector sequence is randomly inserted into the avian genome; and deriving a mature transgenic avian from said transgenic cells, wherein tubular gland cells of the transgenic avian express the protein.

28. The method of claim 27, wherein said promoter is a magnum-specific promoter.

29. The method of claim 27, wherein said promoter is a constitutive promoter.

30. The method of claim 29, further comprising: providing a second vector, wherein said second vector comprises a second coding sequence and a magnum-specific promoter operably linked to said second coding sequence; and expressing said second vector in the tubular gland cells of the transgenic avian, wherein the expression of said first coding sequence is directly or indirectly dependent upon the cellular presence of the protein expressed by the second coding sequence.

31. The method of claim 30, wherein said second coding sequence encodes for Cre and the first vector further comprises a *loxP*-bounded blocking sequence which prevents expression of the first protein-encoding nucleic acid sequence in the absence of Cre.

5 32. The method of claim 30, wherein said second coding sequence encodes FLP recombinase and the first vector further comprises an FRT-bounded blocking sequence which prevents expression of the first coding sequence in the absence of FLP recombinase.

10 33. The method of claim 27, wherein the introduction of the vector into the blastodermal cells is mediated by a retrovirus.

15 34. The method of claim 33, wherein the step of introducing said vector to the embryonic blastodermal cells includes administering helper cells to an embryonic blastoderm, wherein said helper cells produce the retrovirus.

35. A method for producing an avian egg which contains exogenous protein, comprising:

20 providing a vector that comprises a coding sequence and a promoter operably linked to said coding sequence, wherein said promoter can effect expression of the coding sequence in the tubular gland cells of an avian oviduct;

15 creating transgenic cells by introducing said vector into avian embryonic blastodermal cells, wherein the vector sequence is randomly inserted into the avian genome; and

25 deriving a mature transgenic avian from said transgenic cells, wherein the tubular gland cells of the transgenic avian express the coding sequence, and the resulting protein is secreted into the oviduct lumen, so that the protein is deposited <sup>in the white</sup> onto the yolk of an egg.

36. A method for the stable introduction of an exogenous nucleic acid sequence into a target endogenous gene in the avian genome, comprising:

introducing the vector of claim 10 into avian embryonic blastodermal cells, wherein said vector is integrated into the target endogenous gene.

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37. A method for producing an exogenous protein in specific cells of an avian, comprising:

creating transgenic cells by introducing the vector of claim 10 into avian embryonic blastodermal cells, wherein said target gene is an endogenous gene that is expressed in said specific cells and said vector is integrated into the target endogenous gene in the embryonic blastodermal cells; and

10 deriving a mature transgenic bird from said transgenic cells, wherein the coding sequence is expressed in the specific cells of the transgenic bird under the control of the regulatory elements of the target gene.

15 38. The method of claim 38, wherein said specific cells are tubular gland cells.

39. A method for producing an avian egg that contains exogenous protein, comprising:  
creating transgenic cells by introducing the vector of claim 10 into avian embryonic blastodermal cells, wherein said target gene is an endogenous gene that is expressed in tubular gland cells and said vector is integrated into the target endogenous gene; and

20 25 deriving a mature transgenic bird from said transgenic cells, wherein the coding sequence is expressed in the magnum under the control of the regulatory sequences of the target gene and the exogenous protein is secreted into the oviduct lumen, so that the exogenous protein is deposited onto the yolk of an egg.

40. A vector comprising a coding sequence and a promoter derived from the *lysozyme* promoter region in operational and positional relationship to express said coding sequence in tubular gland cells of the avian oviduct.

5 41. An egg of claim 25, wherein said protein is selected from the group consisting of human growth hormone, interferon,  $\beta$ -casein,  $\alpha$ -1 antitrypsin, antithrombin III, collagen, factors VIII, factor IX, factor X, fibrinogen, hyaluronic acid, insulin, lactoferrin, protein C, erythropoietin (EPO), granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage colony-stimulating factor (GM-CSF), tissue-type plasminogen activator (tPA), feed additive enzymes, somatotropin, and chymotrypsin.

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